

Amendments to the Specification

Please replace paragraph [0072] beginning on page 40 with the following amended paragraph:

To inhibit nitric oxide activity, perfluorocarbons are administered in amounts of at least about 0.5% w/v of total blood, or more. To potentiate nitric oxide activity, perfluorocarbons are administered in amount of less than about 0.5% w/v of blood. To enhance nitric oxide even further, a nucleophile is administered in conjunction with or shortly before or after administration of the perfluorocarbon.

Additionally, the patient is irradiated with light of a visible wavelength.

Please replace paragraph [0118] beginning on page 40 with the following amended paragraph:

If delivered at small concentrations, i.e., less than 1% v/v, and in conjunction with low molecular weight nucleophiles, such as thiols or mixtures of thiols, perfluorocarbons act as a powerful vasodilator rather than as a vasoconstrictor. This effect is due to micellar catalysis of vasoactive S-nitrosothiols formation by perfluorocarbons, as shown in Figures 3, 5, and 6.  $\text{NO}^+$  originated from  $\text{N}_2\text{O}_3$  in the perfluorocarbon micelles can be transferred to various low molecular weight nucleophiles, exemplified as RSH, by two possible pathways, as shown in Figure 7. Direct attack on RSH

is possible at the surface of perfluorocarbon micelles or inside the micelles, if the RSH were hydrophobic enough to enter it, as shown in pathway I of Figure 7. Additionally,  $\text{NO}^+$  can reach various RSH via a transnitrosation reaction by using a lipophilic low molecular weight "shuttle", as shown in Figure 7. One example of such an  $\text{NO}^+$  shuttle is  $\alpha$ -lipoic acid ( $\alpha$ -LA), which is normally present in the circulation at low (micromolar) concentrations (Keipert, 2001).  $\alpha$ -lipoic acid has a highly hydrophobic tail (Figure 7A), which can readily penetrate the perfluorocarbon micelle where it is nitrosated. Since both SH groups of  $\alpha$ -dihydro-lipoic acid are located next to each other, upon nitrosation they would almost immediately form an S-S adduct and release  $\text{NO}^+$ . Thus,  $\alpha$ -lipoic acid may serve as a shuttle to transfer  $\text{NO}^+$  from the perfluorocarbon micelle interior to outside hydrophilic low molecular weight RSH thus potentiating the PFC-mediated RS-NO formation (Figure 7B). Our *in vitro* and *in vivo* results support this conclusion (Figure 8). Since low molecular weight S-nitrosothiols are potent vasodilators and anticoagulants, they are regarded as promising cardiovascular therapeutics (Hogg, 2000; Al-Sa-doni et al., 2000; Richardson, et al., 2002). However, the major drawback of available low molecular weight S-nitrosothiols is that they are very unstable in physiological vehicles. Moreover, high doses of S-nitrosothiols can be toxic and

dangerously affect blood flow. Therefore, the use of stable and safe RSH, such as GSH, cysteine, and  $\alpha$ -lipoic acid in conjunction with perfluorocarbons to achieve the same effects as that of corresponding exogenous S-nitrosothiols should be advantageous.